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T. WALLACE

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PTO/SB/16 (8-00)
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PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Adi	LORIAN	25 Shderot Sapir Tiberias, ISRAEL

[X] Additional inventors are being named on the 2 separately numbered sheets attached hereto.

TITLE OF THE INVENTION (280 characters max)

SURGICAL TOOLS AND TECHNIQUES FOR STIMULATION

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

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OR

[X] Firm or Individual Name	ABELMAN, FRAYNE & SCHWAB Attorneys at Law				
Address	150 East 42nd Street				
Address	New York, New York 10017				
City		State		Zip	
Country	U.S.A.	Telephone	(212) 949-9022	Fax	(212) 949-9190

ENCLOSED APPLICATION PARTS (*check all that apply*)

[X] Specification	Number of Pages	28	[ ] CD(s), Number	
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[ ] Application Data Sheet. See 37 CFR 1.76				

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT (check one)

[X] Applicant claims small entity status. See 37 CFR 1.27.

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[ ] Yes, the name of the U.S. Government agency and the Government contract number are: ______

Respectfully submitted,

SIGNATURE Jay S. Cinamon

TYPED or PRINTED NAME Jay S. Cinamon

TELEPHONE (212) 949-9022

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PROVISIONAL APPLICATION COVER SHEET
Additional Page

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Docket Number	205,961	Type a plus sign (+) inside this box →	+

INVENTOR(S) APPLICANT(S)		
Given Name (first and middle (if any)	**Family or Surname**	**Residence (City and either State or Foreign Country)**
Yossi	GROSS	10 HaNotea Street Moshav Mazor, ISRAEL
Alon	SHALEV	9 Wingate Street Ra'anana, ISRAEL
Raphael	BENARY	15 HaRav Ashi Street Tel Avi, ISRAEL

SURGICAL TOOLS AND TECHNIQUES FOR STIMULATION

CROSS-REFERENCES TO RELATED APPLICATIONS

This application is related to: (i) a US regular patent application to Gross et al., filed on even date herewith, entitled, "Stimulation for treating eye pathologies," and (ii) a US provisional patent application to Gross et al., filed on even date herewith, entitled, "Stimulation circuitry and control of electronic medical device."

Each of the above-cited patent applications is assigned to the assignee of the present patent application and is incorporated herein by reference.

FIELD OF THE INVENTION

The present invention relates generally to medical procedures and electronic devices. More specifically, the invention relates to the use of electrical devices for implantation in the head and surgical techniques for implanting the devices.

BACKGROUND OF THE INVENTION

The blood-brain barrier (BBB) is a unique feature of the central nervous system (CNS), which isolates the brain from the systemic blood circulation. To maintain the homeostasis of the CNS, the BBB prevents access to the brain for many substances circulating in the blood.

The BBB is formed by a complex cellular system of endothelial cells, astroglia, pericytes, perivascular macrophages, and a basal lamina. Compared to other tissues, brain endothelia have the most intimate cell-to-cell connections: endothelial cells adhere strongly to

each other, forming structures specific to the CNS called "tight junctions" or zonula occludens. They involve two opposing plasma membranes, which form a membrane fusion with cytoplasmic densities on either side. These tight junctions prevent cell migration or cell movement between endothelial cells. A continuous uniform basement membrane surrounds the brain capillaries. This basal lamina encloses contractile cells called pericytes, which form an intermittent layer and probably play some role in phagocytosis activity and defense if the BBB is breached. Astrocytic end feet, which cover the brain capillaries, build a continuous sleeve and maintain the integrity of the BBB by the synthesis and secretion of soluble growth factors (e.g., gamma-glutamyl transpeptidase) essential for the endothelial cells to develop their BBB characteristics.

Because of the BBB, certain non-surgical treatments of the brain based upon systemic introduction of compounds through the bloodstream have been ineffective or less effective. For example, chemotherapy has been relatively ineffective in the treatment of CNS metastases of systemic cancers (e.g., breast cancer, small cell lung cancer, lymphoma, and germ cell tumors) despite clinical regression and even complete remission of these tumors in non-CNS systemic locations. The most important factors determining drug delivery from blood into the CNS are lipid solubility, molecular mass, and electrical charge. A good correlation exists between the lipid solubility of a drug, expressed as the octanol/water partition coefficient, and the drug's ability to penetrate or diffuse across the BBB. This is particularly relevant for drugs with molecular weights smaller than 600 Dalton (Da). The normal BBB prevents the passage of ionized water soluble drugs with molecular weight greater than

180 Da. Most currently available effective chemotherapeutic agents, however, have a molecular weight between 200 and 1200 Da. Therefore, based both on their lipid solubilities and molecular masses, the passage of many agents is impeded by the BBB.

In addition to transcellular diffusion of lipophilic agents, there are several specific transport mechanisms to carry certain molecules across the brain's endothelial cells. Specific transport proteins exist for required molecules, such as glucose and amino acids. Additionally, absorptive endocytosis and transcytosis occur for cationized plasma proteins. Specific receptors for certain proteins, such as transferrin and insulin, mediate endocytosis and transport across the cell.

Non-surgical treatment of neurological disorders is generally limited to systemic introduction of compounds such as neuropharmaceuticals and other neurologically active agents that might remedy or modify neurologically related activities and disorders. Such treatment is limited, however, by the relatively small number of known compounds that pass through the BBB. Even those that do cross the BBB often produce adverse reactions in other parts of the body or in non-targeted regions of the brain.

There have been a number of different studies regarding efforts to cross the BBB, specifically with regard to overcoming the limited access of drugs to the brain. Such efforts have included, for example, chemical modification, development of more hydrophobic analogs, or linking an active compound to a specific carrier. Transient opening of the BBB in humans has been achieved by intracarotid infusion of hypertonic mannitol solutions or bradykinin analogs. Also, modulation of the P-

glycoprotein, whose substrates are actively pumped out of brain cells into capillary lumens, has been found to facilitate the delivery of drugs to the brain.

The sphenopalatine ganglion (SPG) is a neuronal center located in the brain behind the nose. It consists of parasympathetic neurons innervating the middle cerebral and anterior cerebral lumens, the facial skin blood vessels, and the lacrimal glands. Activation of this ganglion is believed to cause vasodilation of these vessels. A second effect of such stimulation is the opening of pores in the vessel walls, causing plasma protein extravasation (PPE). This effect allows better transport of molecules from within these blood vessels to surrounding tissue.

The middle and anterior cerebral arteries provide the majority of the blood supply to the cerebral hemispheres, including the frontal and parietal lobes in their entirety, the insula and the limbic system, and significant portions of the following structures: the temporal lobes, internal capsule, basal ganglia and thalamus. These structures are involved in many of the neurological and psychiatric diseases of the brain. Currently the SPG is a target of manipulation in clinical medicine, mostly in attempted treatments of severe headaches, such as cluster headaches. The ganglion is blocked either on a short-term basis, by applying lidocaine, or permanently, by ablation with a radio frequency probe. In both cases the approach is through the nostrils.

The following references, which are incorporated herein by reference, may be useful:

Delepine, L., Aubineau, P., "Plasma protein extravasation induced in the rat dura mater by

stimulation of the parasympathetic sphenopalatine ganglion," Experimental Neurology, 147, 389-400 (1997).

Hara, H., Zhang, Q. J., Kuroyanagi, T., Kobayashi, S., "Parasympathetic cerebrovascular innervation: An anterograde tracing from the sphenopalatine ganglion in the rat," Neurosurgery, 32, 822-827 (1993).

Jolliet-Raint, P., Tillement, J. P., "Drug transfer across the blood-brain barrier and improvement of brain delivery," Fundam. Clin. Pharmacol., 13, 16-25 (1999).

Kroll, R. A., Neuwelt, E. A., "Outwitting the blood brain barrier for therapeutic purposes: Osmotic opening and other means," Neurosurgery, 42, 1083-1100 (1998).

Sanders, M., Zuurmond, W. W., "Efficacy of sphenopalatine ganglion blockade in 66 patients suffering from cluster headache: A 12-70 month follow-up evaluation," Journal of Neurosurgery, 87, 876-880 (1997).

Seylaz, J., Hara, H., Pinard, E., Mraovitch, S., MacKenzie, E. T., Edvinsson, L, "Effects of stimulation of the sphenopalatine ganglion on cortical blood flow in the rat," Journal of Cerebral Blood Flow and Metabolism, 8, 875-878 (1988).

Van de Waterbeemd, H., Camenisch, G., Folkers, G., Chretien, J. R., Raevsky, O. A., "Estimation of blood brain barrier crossing of drugs using molecular size and shape and h bonding descriptors," Journal of Drug Targeting, 6, 151-165 (1998).

Suzuki, N., Hardebo, J. E., Kahrstrom, J., Owman, C., "Selective electrical stimulation of postganglionic cerebrovascular parasympathetic nerve fibers originating from the sphenopalatine ganglion enhances cortical blood flow in the rat," Journal of Cerebral Blood Flow and Metabolism, 10, 383-391 (1990).

Suzuki, N., Hardebo, J. E., Kahrstrom, J., Owman, C. H., "Effect on cortical blood flow of electrical stimulation of trigeminal cerebrovascular nerve fibres in the rat," Acta Physiol. Scand., 138, 307-315 (1990).

PCT Patent Publication WO 01/85094 to Shalev and Gross, which is assigned to the assignee of the present patent application and whose disclosure is incorporated herein by reference, describes methods and apparatus for stimulating the sphenopalatine ganglion to modify properties of the blood brain barrier and cerebral blood flow for the treatment of medical conditions. Treatment is accomplished directly via stimulation of the sphenopalatine ganglion and/or indirectly by the facilitation of drug transport across the blood brain barrier via stimulation of the sphenopalatine ganglion.

PCT Patent Publication WO 01/97905 to Ansarinia, whose disclosure is incorporated herein by reference, describes a method for treating a patient by placing at least one electrode on or proximate to at least one of the patient's sphenopalatine ganglia, sphenopalatine nerves, or vidian nerves, and activating the electrode to apply an electrical signal and/or a medical solution to at least one of those ganglia or nerves.

U.S. Patent 6,405,079 to Ansarinia, whose disclosure is incorporated herein by reference, describes methods for treating medical conditions by implanting one or more electrodes in regions of the sinus and applying electrical stimulation and/or medical solutions to the implantation site.

SUMMARY OF THE INVENTION

It is an object of some aspects of the present invention to provide improved methods and apparatus for surgically implanting apparatus in a region adjacent to the sphenopalatine ganglion.

It is also an object of some aspects of the present invention to provide improved methods and apparatus for delivery of compounds to the brain, particularly through the BBB.

It is also an object of some aspect of the present invention to provide such methods and apparatus as can be employed to deliver such compounds through the BBB with a minimally-invasive approach.

It is a further object of some aspects of the present invention to provide methods and apparatus as can facilitate delivery of large molecular weight compounds through the BBB.

It is yet a further object of some aspects of the present invention to provide improved methods and apparatus for remedying or modifying neurological activities and disorders via delivery of compounds through the blood brain barrier.

It is still a further object of some aspects of the present invention to modulate cerebral blood flow.

It is also a further object of some aspects of the present invention to provide improved methods and apparatus for treating stroke.

It is an additional object of some aspects of the present invention to provide improved methods and apparatus for treating migraine.

It is yet an additional object of some aspects of the present invention to provide improved methods and apparatus for treating neurological diseases (for example, Alzheimer's disease), whose prognosis and evolution of pathological symptoms are influenced by cerebral blood flow.

It is still an additional object of some aspects of the present invention to provide implantable apparatus that affects the brain, without actually being implanted in the brain. In particular, the apparatus may be implanted in a region adjacent to the sphenopalatine ganglion.

In some preferred embodiments of the present invention, apparatus for stimulating the "sphenopalatine ganglion (SPG) system" (defined below) is surgically implanted so as to stimulate the SPG system. Preferably, the surgical procedure is performed in a relatively minimally-invasive manner to reduce patient discomfort during and after the procedure. Once implanted, the apparatus typically delivers the energy to the SPG system in order to control and/or modify SPG-related behavior, e.g., in order to induce changes in cerebral blood flow and/or to modulate permeability of the blood-brain-barrier (BBB). These embodiments may be used in many medical applications, such as, by way of illustration and not limitation, (a) the treatment of cerebrovascular disorders such as stroke, (b) the treatment of migraine headaches, (c) the treatment of Alzheimer's disease, (d) the facilitation of drug transport across the BBB, and/or (e) the facilitation of extraction of analytes from the brain.

In the present patent application, including the claims, "SPG system" means the SPG and associated

neuroanatomical structures, including neural tracts originating in or reaching the SPG, including outgoing and incoming parasympathetic and sympathetic tracts, which tracts include preganglionic fibers of the SPG (fibers contained within the vidian nerve) and postganglionic fibers of the SPG (fibers that travel anterogradely from the SPG toward the brain vascular bed, including the anterior and posterior ethmoidal nerves, and including the retro-orbital branches of the SPG, which are fibers that connect the SPG with orbital neural structures).

It is to be appreciated that, in general, the techniques described herein may be applied directly, or applied with changes *mutatis mutandis*, so as to facilitate stimulation of one or more of the following and thereby facilitate treatment of a medical condition:

- a sphenopalatine ganglion (SPG) (also called a pterygopalatine ganglion);
- an anterior ethmoidal nerve;
- a posterior ethmoidal nerve;
- a communicating branch between the anterior ethmoidal nerve and the SPG (retro-orbital branch);
- a communicating branch between the posterior ethmoidal nerve and the SPG (retro-orbital branch)
- a nerve of the pterygoid canal (also called a vidian nerve), such as a greater superficial petrosal nerve (a preganglionic parasympathetic nerve)

or a lesser deep petrosal nerve (a postganglionic sympathetic nerve);

- a greater palatine nerve;
- a lesser palatine nerve;
- a sphenopalatine nerve;
- a communicating branch between the maxillary nerve and the sphenopalatine ganglion;
- a nasopalatine nerve;
- a posterior nasal nerve;
- an infraorbital nerve;
- an otic ganglion;
- an afferent fiber going into the otic ganglion; and/or
- an efferent fiber going out of the otic ganglion.

According to a preferred embodiment of the present invention, a method and apparatus are provided to facilitate placement of at least one electrode adjacent to the sphenopalatine ganglion via an endoscopic transpalatine approach to the sphenopalatine ganglion. Preferably, local anesthetic is applied to the oral palatine mucosa and a greater palatine block is performed prior to a mucoperiosteal incision proximate the greater palatine foramen to reveal the contents of the foramen. A trocar comprising a flexible guide tube is preferably inserted vertically through the incision to provide access for endoscopic dissection and visualization tools, which are used for the subsequent portion of the procedure. Preferably, the endoscopic tools are used for

subperiosteal dissection to detach the greater palatine canal contents from the osseous part of the canal and provide access to the vidian foramen and a portion of the SPG.

Preferably, at least one electrode is placed next to or in contact with the SPG via the flexible guide tube. In a preferred embodiment, each electrode is flat so as to provide a large contact area between the electrode and SPG. Preferably, the electrode is flexible enough to be rolled up and inserted through the trocar and guide tube and sufficiently elastic to resume a generally planar shape once through the trocar and guide tube. Additionally or alternatively, the electrode has a curved shape such that it may be hooked around a nerve in the SPG system, such as the vidian nerve.

Typically, the at least one electrode comprises two or more electrodes, driven to operate in a multi-polar mode (e.g., in a bipolar mode for the case of two electrodes).

Subsequent to placement of the at least one electrode, proper placement is preferably assured by running a test current through the at least one electrode and monitoring the physiological effect on the patient. Preferably, once proper placement of the at least one electrodes is assured, the electrodes are coupled to a control unit. In a preferred embodiment, the control unit is implanted in the patient. Alternatively, an external control unit is used to control the at least one electrode.

According to another preferred embodiment of the present invention, a method and apparatus are provided to facilitate placement of at least one electrode adjacent to the sphenopalatine ganglion via a combined trans-

maxillary sinus and trans-nasal endoscopic assisted approach. Preferably, after administration of appropriate anesthesia, the posterior wall of the maxillary sinus is carefully dissected and the anterior part of the sphenopalatine fossa is dissected via a trans-maxillary approach. The dissection is preferably performed approximately 0.5 mm from the medial wall of the maxillary sinus, under direct endoscopic visualization. Subsequently, a complete nasal endoscopic examination is preferably performed on both sides, and then, under direct visualization, an incision is made about 0.4 mm - about 0.8 mm under the second conchae on the operating side. Preferably, a mucoperiosteal flap is raised posteriorly and inferiorly, to allow the sphenopalatine artery to be dissected and clamped. The sphenopalatine fossa is then preferably approached under direct endoscopic visualization, and the lateral wall of the nose is penetrated. Subsequently, in a preferred embodiment, the sphenopalatine ganglion is approached via the maxillary sinus. In another preferred embodiment, the sphenopalatine ganglion is accessed via a trans-nasal approach.

Preferably, an introducer, comprising a hollow tube, is inserted through the dissected tissue to provide a pathway for introduction of the at least one electrode, which comprises a lead wire, to a region adjacent to the sphenopalatine ganglion. In a preferred embodiment the electrodes are flat, such that a large surface area is available for contact with the sphenopalatine ganglion. In another preferred embodiment, one or more of the electrodes are curved, so as to wrap around a portion of a nerve such as the vidian nerve, or another nerve in the SPG system.

Once the at least one electrode is placed, a controlled stimulation is preferably performed by passing a current through the lead wire to the electrode to confirm that the electrode is properly placed. Evaluation of the proper placement of the at least one electrode comprises one or more of: (1) evaluating the vasodilatation of blood vessels in the eye, (2) assessment of cerebral blood flow by using a transcranial Doppler, (3) assessment of forehead perfusion by using Laser Doppler, and (4) assessment of forehead perfusion by a temperature sensor. In a preferred embodiment, once proper placement of the electrodes has been verified, the electrodes are coupled to an implantable control unit. In another preferred embodiment, the electrodes are coupled to an external control unit by wired or wireless means.

The present invention will be more fully understood from the following detailed description of the preferred embodiments thereof, taken together with the drawings in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a pictorial illustration of the roof of the oral cavity, showing a site for an incision, in accordance with a preferred embodiment of the present invention;

Fig. 2 is a schematic illustration of endoscopic apparatus for accessing the SPG system, in accordance with a preferred embodiment of the present invention;

Fig. 3 is a pictorial illustration of an endoscopic tool accessing the SPG system, in accordance with a preferred embodiment of the present invention;

Figs. 4A and 4b are schematic illustrations of an electrode introducer for placing an electrode in the SPG system, in accordance with a preferred embodiment of the present invention;

Figs. 5A, 5B, and 5C are schematic illustrations of electrode supports to be placed in the SPG system, in accordance with preferred embodiments of the present invention;

Fig. 6 is a schematic illustration of an electrode to be hooked around a nerve in the SPG system, in accordance with a preferred embodiment of the present invention;

Fig. 7 is a schematic illustration of an endoscopic tool for placing an electrode in the SPG system, in accordance with a preferred embodiment of the present invention;

Fig. 8 is a schematic illustration of a system for supporting electrical leads during placement of an electrode in the SPG system, in accordance with a preferred embodiment of the present invention;

Figs. 9A and 9B are schematic, partly sectional illustrations of receivers for receiving control and power signals to drive an electrode that is placed in the SPG system, in accordance with a preferred embodiment of the present invention;

Fig. 10 is a schematic, partly sectional illustration of the placement of an electrode in the SPG system and a control unit on the upper jaw, in accordance with a preferred embodiment of the present invention; and

Fig. 11 is a schematic pictorial illustration of the placement of an electrode adjacent to the anterior ethmoidal nerve and a control unit on the orbital rim, in accordance with a preferred embodiment of the present invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Fig. 1 is a schematic, pictorial illustration showing a roof of the oral cavity 20 and associated anatomical structures, where dissection commences in a surgical procedure to access the sphenopalatine ganglion system, in accordance with a preferred embodiment of the present invention. In this preferred embodiment, soft tissue is dissected to expose the greater palatine foramen 22, in order to allow access via the pterygopalatine canal to the SPG system by means of an endoscopic transpalatine approach.

To start the procedure, the patient is preferably positioned with an open mouth, and a topical and local anesthetic is applied to the oral palatine mucosa. After the local anesthetic has taken the desired effect (typically about 2 - 3 minutes) a greater palatine nerve block is preferably performed. The greater palatine foramen 22 is then located, preferably by the anatomical landmark of the second upper molar 24. Preferably, a mucoperiosteal incision is made in front of the location of the greater palatine foramen, and the contents of the foramen are dissected and revealed.

Fig. 2 is a schematic illustration showing endoscopic apparatus 30, which is used in the surgical procedure to access the SPG once the contents of the greater palatine foramen have been dissected and revealed, in accordance with a preferred embodiment of the present invention. Apparatus 30 comprises a handle 38, which contains a keyhole opening 42, through which a flexible hollow sleeve 36 is placed. Preferably sleeve 36 serves as a conduit and guide for introduction of endoscopic tools, while handle 38 is used to move and

orient sleeve 36 and any introduced endoscopic tools. Further preferably, sleeve 36 comprises a slit 43, running the length of the sleeve, which is lined up with keyhole opening 42, such that handle 38 and sleeve 36 can be removed from around wires subsequently introduced through the sleeve.

In some preferred embodiments of the present invention, hollow sleeve 36 is adapted to permit a flexible shaft 34 to be introduced and advanced to a desired operative site. Flexible shaft 34 is preferably adapted such that a surgical tool 40 may be attached to the distal end of the shaft. For example, Fig. 2 shows a surgical tool comprising a periosteal elevator. In some preferred embodiments of the present invention, flexible shaft 34 is hollow so as to allow the introduction of additional apparatus to the operative site. Fig. 2 shows a preferred embodiment in which a trocar 32 is introduced through hollow flexible shaft 34.

Preferably, endoscopic apparatus 30 is used to proceed with the surgical procedure subsequent to dissection of the contents of the greater palatine foramen, by inserting hollow sleeve 36 into the greater palatine foramen with the aid of handle 38. Once the hollow sleeve is suitably positioned, flexible shaft 34 with attached surgical tool 40 and trocar 32 are preferably inserted through hollow sleeve 36. In a preferred embodiment, surgical tool 40 comprises a periosteal elevator. Trocar 32 is preferably advanced using a gentle 180 degree axial rotation, and subperiosteal dissection is performed with the aide of surgical tool 40 so as to detach the contents of the greater palatine canal from the osseous portion of the canal. Preferably, the dissection is monitored with

endoscopic visualization, while irrigation and suction are used as necessary to maintain the site of dissection. Trocar 32 should preferably be introduced about 2 centimeters relative to the bony entrance of the greater palatine canal, with allowable variation for the anatomy of individual patients.

Fig. 3 illustrates shaft 34 and the anatomy of the pterygopalatine fossa 50, which shows the sphenopalatine ganglion 52 adjacent to the sphenopalatine artery 54, in accordance with a preferred embodiment of the present invention. The vidian nerve 57, contained in the vidian foramen 56, is seen to be connected to the sphenopalatine ganglion 52. Preferably, the vidian foramen and nerve are approached under direct endoscopic visualization, after the steps described hereinabove with reference to Fig. 2. Preferably, hollow flexible shaft 34 (see also Fig. 2) is introduced towards vidian nerve 57 and/or sphenopalatine ganglion 52.

Fig. 4A shows an electrode introducer 60, comprising a flexible rod 62, to which an electrode support 58 is attached, and a handle 64 for manipulating the introducer, in accordance with a preferred embodiment of the present invention. Preferably, electrode support 58 is introduced to the region of the vidian nerve and the sphenopalatine ganglion via flexible shaft 34.

Fig. 4B shows a flexible electrode support 58, rolled to fit inside shaft 34, at a point in time as support 58 is advanced out from shaft 34, such that support 58 opens upon exiting the distal end of shaft 34, in accordance with a preferred embodiment of the present invention. Electrodes 66a are affixed to one or more sites on the electrode support, and are positioned to be

in contact with a target site such as the SPG when the support unrolls.

Figs. 5A, 5B, and 5C show several electrode configurations for use with electrode support 58, in accordance with respective preferred embodiments of the present invention. The three illustrated electrode configurations are typically flat, providing a relatively large surface area for contact with the SPG or other tissue. Additionally, the flexibility and flat thin shapes of the electrode support and the electrodes are conducive to being rolled up, for some applications, so as to fit through flexible shaft 34 and subsequently return to essentially their initial flat shape (see Fig. 4b). Fig. 5a shows a simple plate electrode design comprising two plates 66a, which are each connected to respective leads 65, preferably but not necessarily by laser welding. Other preferred embodiments comprise more than two plates 66a. Preferably, plates 66a comprise platinum/iridium or other suitable substances known in the art of tissue stimulation.

Fig. 5B shows an alternate electrode design where each of two compound plate electrodes 66b preferably comprises a horizontal strip 67, to which a plurality of vertical plates 69 is coupled. Preferably, each horizontal strip 67 is coupled to a respective lead 65 by laser welding. Horizontal strip 67 and vertical plates 69 preferably comprise platinum/iridium or other suitable substances known in the art of tissue stimulation.

Fig. 5C shows another electrode design providing a large surface area for contact with the SPG, comprising two shaped electrodes 66c, which are shaped to provide the desired electrical stimulation to the SPG. In a preferred embodiment, electrodes 66c are formed by

cutting the shapes out of a simple plate comprising platinum/iridium or other suitable substances known in the art of tissue stimulation.

For some applications, electrode support 58 shown in Figs. 5A, 5B, and 5C is about 4 mm by about 6-10 mm. The total contact surface area between the SPG (or other tissue) and the electrodes in these figures is, in some embodiments, between about 0.5 mm2 and about 2 mm2.

Fig. 6 shows an electrode 68 that is configured to wrap around a nerve, in accordance with a preferred embodiment of the present invention. Electrode 68 is shown in the figure a bipolar configuration, for placement at respective longitudinal sites on the nerve. For some applications, electrode 68 comprises a single monopolar "hook" electrode. Preferably, electrode 68 comprises two conductive strips 70, pre-bent to a curved shape such that they can be placed during a procedure to wrap around a target nerve, for example the vidian or ethmoidal nerves. The inner portion of conductive strips 70 is designated to be in contact with the target nerve (or only marginally separated therefrom), and provides the electrical stimulation to the nerve. The outer surfaces of strips 70, i.e., those not in contact with the nerve, are typically sheathed or otherwise coated in a non-conductive material 72, to reduce or eliminate stimulation of tissues surrounding the target nerve.

Fig. 7 shows details of flexible rod 62 (see Figs. 4A and 4B), which is used in the placement of electrode support 58 and comprises one or more electrical leads 74 for transmitting electrical power to the electrodes (e.g., electrodes 66a) on electrode support 58, in accordance with a preferred embodiment of the present invention. Preferably, electrical leads 74 are cast into

a solid elastomer sheathing 76 to provide a desired degree of flexibility and strength during the introduction of the electrodes, and to also provide the isolation of the leads from bodily tissues and fluids.

Fig. 8 shows apparatus for supporting and protecting electrical leads 74 while maintaining sufficient strength and flexibility, in accordance with a preferred embodiment of the present invention. Preferably, leads 74 are threaded through a hollow tube 80, chosen to provide appropriate strength and flexibility, which typically comprises a plurality of supports 82 along the length of tube 80 for holding leads 74 and preventing damage to the leads during introduction or operation of the electrodes.

Fig. 9A shows a partially sectional view of a receiver 78, which is adapted to be coupled to the proximal end of rod 62 (Fig. 4A) by a base 92 and to receive power and control signals from a control unit that drives electrodes such as electrodes 66a on electrode support 58, in accordance with a preferred embodiment of the present invention. Receiver 78 comprises a coil 90 and an electronics pod 94, which are coupled to a base 92 and adapted to receive power and drive electrodes 66a. Preferably, coil 90 is constructed using Drawn Filled Tube technology, and typically comprises a combination of MP35N and silver. In a preferred embodiment, coil 90 is adapted to receive control and power inputs wirelessly. By way of example but not limitation, RF electromagnetic fields and/or oscillating magnetic fields are used to wirelessly power and control electrodes 66a via coil 90 and electronics pod 94..

Fig. 9B shows a partially sectional view of a receiver 100, which is adapted to be coupled to the

proximal end of rod 62 (Fig. 4A) by a base 92 and to receive power and control signals from a control unit that drives electrodes such as electrodes 66a on electrode support 58, in accordance with a preferred embodiment of the present invention. Receiver 100 comprises an electronics module 102, which comprises a plurality of connectors 104 for wired connections to a typically non-implanted control unit.

Preferably, receivers 78 and 100 are coated with a non-permeable coating such as, but not limited to, Parylene, which isolates the receiver from physiological fluids and tissues. Further preferably, the receivers are encased in a relatively pliant layer such as an elastomer, which serves as an outer casing for the receiver.

Preferably, once electrode support 58 is properly placed, endoscopic device 30 (see Fig. 2) is removed from the patient, and receiver 78 or receiver 100 remains in the patient, typically immediately above or below the hard palate or at the ridge of the eye, and is connected by leads to the electrodes on electrode support 58. Note that keyhole opening 42 in hollow sleeve 36 and slit 43 in handle 38 allow for the removal of these items without affecting leads 74, because the leads pass through the keyhole and slit as the handle and sleeve are removed. Alternatively, sleeve 36 is made so as to split along its length prior to removal.

Fig. 10 shows the placement of electrode support 58 adjacent to SPG 52 and the placement of a stimulator 112 comprising receiver 78 in the supraperiosteal region of the upper jaw of the patient at midline, in accordance with a preferred embodiment of the present invention. Preferably, stimulator 112 receives power wirelessly from

an external control unit temporarily placed in or near the mouth. Stimulator 112 is typically fixed to the jaw with microscrews. Alternatively, the control unit powers and controls stimulator 112 by a wired connection between the control unit and a receiver 100 (Fig. 9B) incorporated into the stimulator. Further alternatively, one or more lead wires are brought out through the skin and coupled to an external control unit.

Typically, but not necessarily, techniques described in PCT Patent Publication WO 01/85094 to Shalev and Gross, entitled, "Method and apparatus for stimulating the sphenopalatine ganglion to modify properties of the BBB and cerebral blood flow," or the US national phase application thereof, filed October 25, 2002, which are both assigned to the assignee of the present patent application and incorporated herein by reference, are adapted for use with the techniques of these embodiments of the present invention. In particular, electrodes implanted adjacent to the sphenopalatine ganglion, using the relatively minimally-invasive surgical techniques and associated surgical tools of the present invention, are driven by a stimulator (e.g. control unit), using control and driving circuitry and treatment protocols of PCT Patent Publication WO 01/85094, to control the blood brain barrier and/or treat neurological symptoms or disease.

Another preferred embodiment of the present invention comprises a combined trans-maxillary sinus and trans-nasal endoscopic assisted approach to the sphenopalatine ganglion, in order to implant at least one electrode in a region of the sphenopalatine ganglion. Preferably, to start the procedure, the patient is given a local and topical anesthesia in the intraoral

vestibulum at the area of the canine fossa, and a topical intranasal anesthesia at the region of the lateral nasal wall of the operated side. The posterior wall of the maxillary sinus is preferably dissected, and the anterior part of the sphenopalatine fossa is dissected via a trans-maxillary approach. Preferably, the dissection is performed approximately 0.5 mm from the medial wall of the maxillary sinus under direct endoscopic visualization.

Preferably, a complete nasal endoscopic examination is performed on both sides and then under direct visualization an incision is made 0.4-0.8 mm under the second conchae on the operating side. A mucoperiosteal flap is preferably raised posteriorly and inferiorly followed by dissection and clamping of the sphenopalatine artery. Subsequently, under direct visualization, the lateral wall of the nose is preferably penetrated and the sphenopalatine fossa is approached. In a preferred embodiment of the present invention, the surgeon now approaches the sphenopalatine ganglion via the trans-maxillary sinus. In another preferred embodiment, the surgeon approaches the sphenopalatine ganglion via the trans-nasal approach. The specific approach is preferably dependent on the anatomical topography of the patient.

At this stage of the procedure, endoscopic device 30 (see Fig. 2) is preferably inserted in the dissected tissue and used to place an electrode adjacent to the sphenopalatine ganglion, as discussed hereinabove for the endoscopic transpalatine approach to the sphenopalatine ganglion.

Yet another preferred embodiment of the present invention comprises an upper blepharoplasty approach to

the anterior and/or posterior ethmoidal nerves, in order to implant at least one electrode adjacent to the anterior and/or posterior ethmoidal nerves. Preferably, to start the procedure, the patient's upper and lower eyelids are sterilized. A local anesthetic is preferably applied to the upper eyelid. Once the anesthetic has taken effect, an incision in the skin following an eyelid crest is preferably performed. In a preferred embodiment, the incision is approximately 15 mm long.

Once the skin has been dissected, the orbicularis muscle is preferably passed through by performing a blunt dissection. Subsequently, a sharp incision of the periosteum, preferably about 15 mm in length, is made on the superomedial aspect of the orbit. Preferably, the subperiosteal tissue is then dissected to expose the anterior ethmoidal foramen and its contents, including the anterior ethmoidal nerve. Alternatively or additionally, the dissection is performed so as to expose the posterior ethmoidal nerve. Once the anterior and/or posterior ethmoidal nerve has been exposed, at least one electrode is implanted adjacent to the nerve.

Fig. 11 shows the placement of an electrode 120 adjacent to the posterior ethmoidal nerve 124 in the region of the orbital cavity 128, in accordance with a preferred embodiment of the present invention. Preferably, electrode 120 is coupled to a stimulator 122 by a lead 130. Stimulator 122 is preferably fixed to the superior orbital rim. Following placement of electrode 120, lead 130, and stimulator 122, incisions in the periosteum, muscle and skin are closed with standard surgical techniques.

Alternatively, electrode 120 is placed adjacent to anterior ethmoidal nerve 126. Further alternatively, a

plurality of electrodes 120 is placed so as to stimulate both the anterior and the posterior ethmoidal nerves.

Preferably, verification and/or optimization of the electrode nerve interface after the electrodes are placed is performed by observing the effects of stimulation on one or more physiological responses. Potential observations include, but are not limited to: (1) evaluating the vasodilatation of blood vessels of the eye, (2) assessment of cerebral blood flow by using trans-cranial Doppler, (3) assessment of forehead perfusion by using Laser-Doppler, and (4) assessment of forehead perfusion by a temperature sensor.

In some embodiments, techniques described herein are practiced in combination with techniques described in one or both of the following co-assigned US applications: (i) a US regular patent application to Gross et al., filed on even date herewith, entitled, "Stimulation for treating eye pathologies," and (ii) a US provisional patent application to Gross et al., filed on even date herewith, entitled, "Stimulation circuitry and control of electronic medical device." Both of these applications are incorporated herein by reference.

It is noted that the figures depicting preferred embodiments of the present invention are not necessarily drawn to scale, and, instead, may change certain dimensions in order to more clearly demonstrate some aspects of the invention.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and

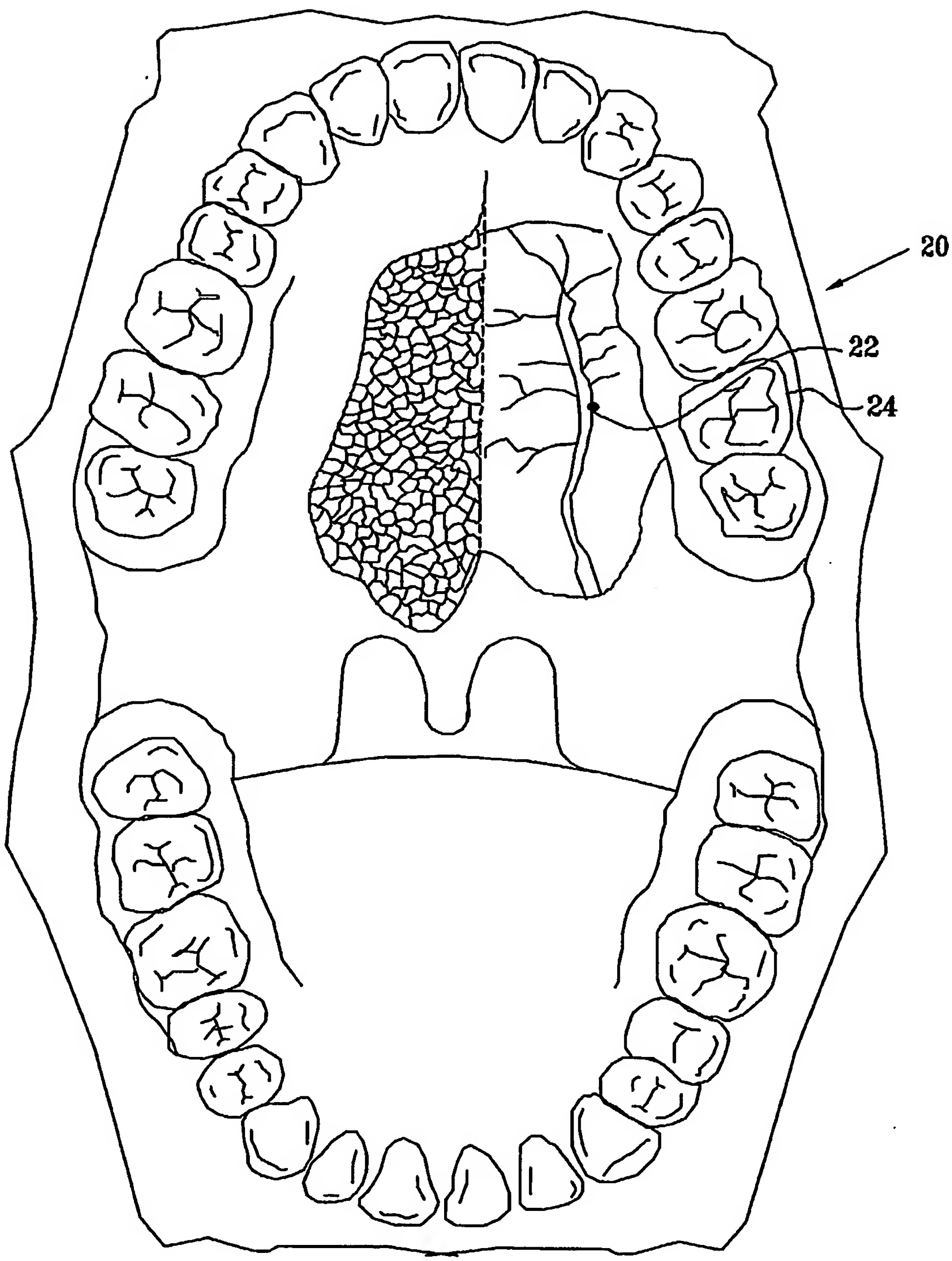
modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.

CLAIMS

1. A method for implanting a device in a region of a sphenopalatine ganglion of a subject, comprising passing the device through a greater palatine foramen of the subject.

2. A method according to claim 1, wherein passing the device comprises passing an electrode through the greater palatine foramen.

FIG. 1



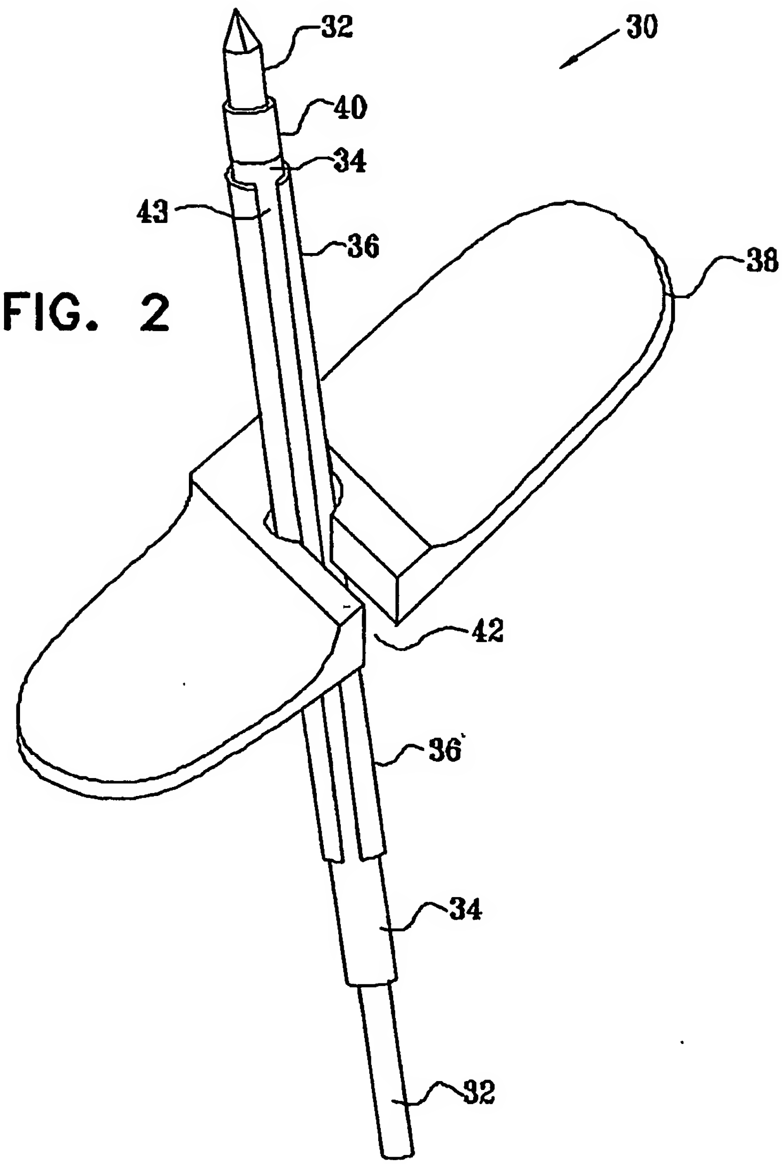


FIG. 2

FIG. 3

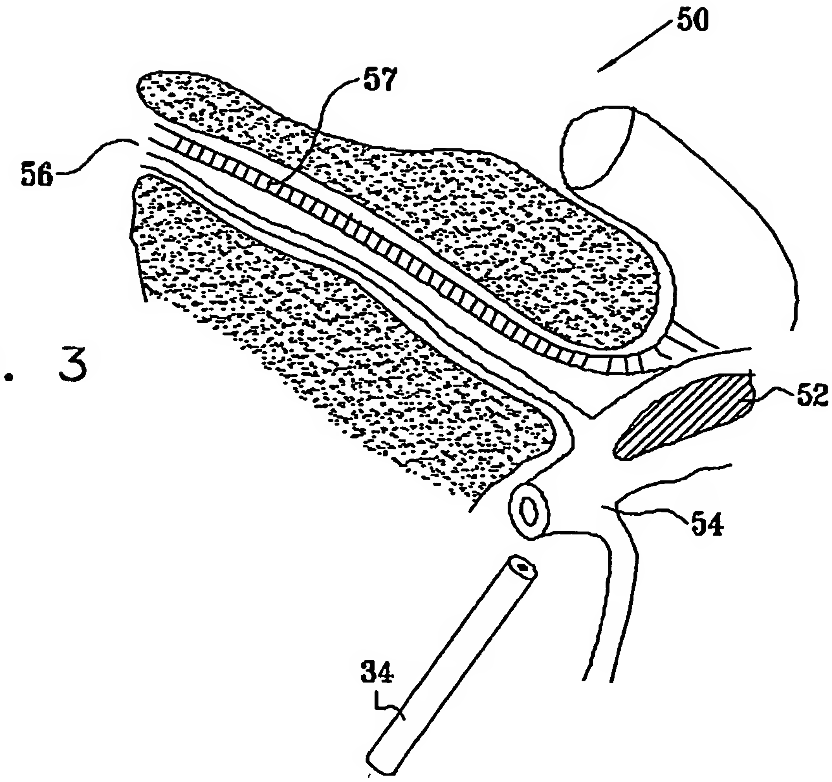
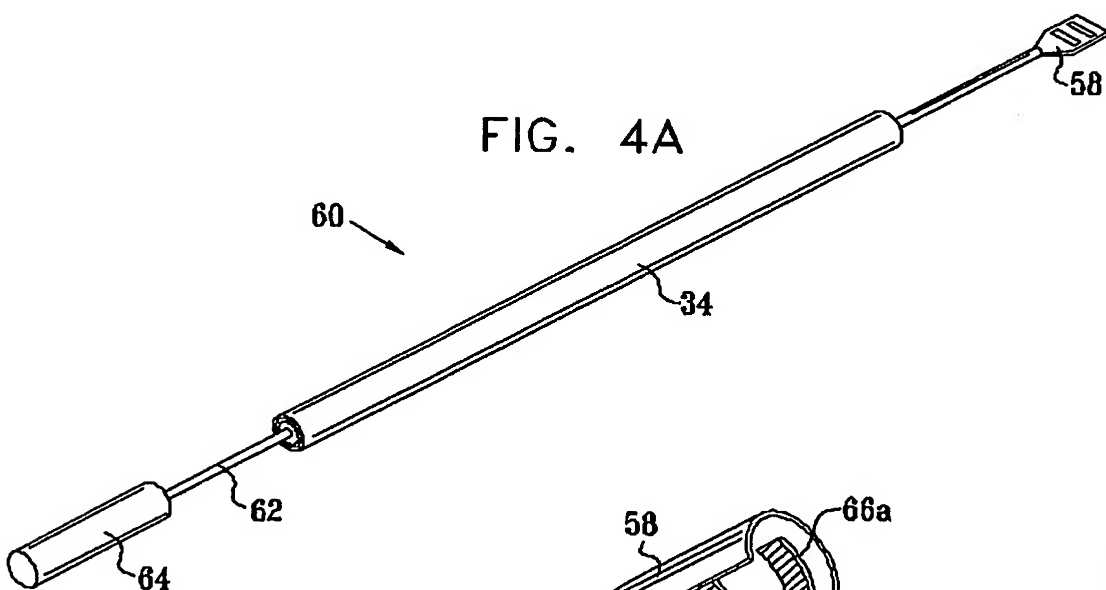


FIG. 4A



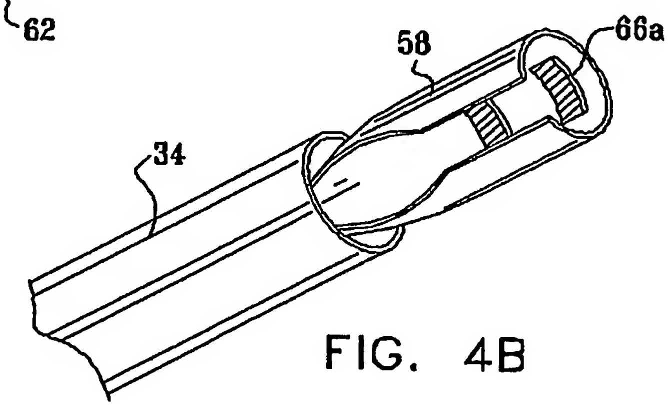


FIG. 4B

FIG. 5A

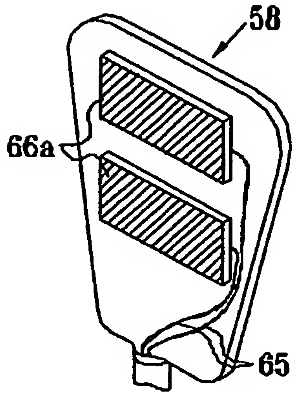


FIG. 5B

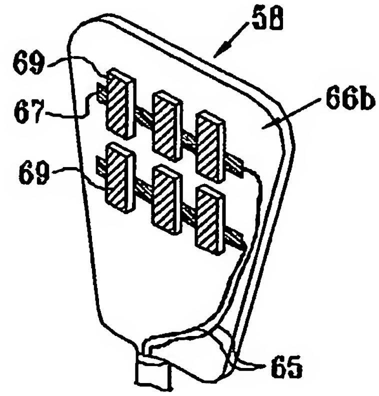


FIG. 5C

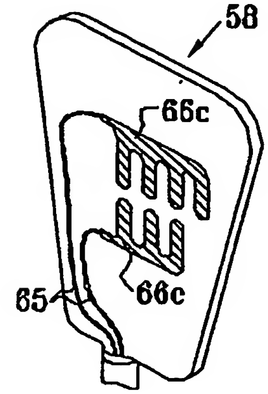


FIG. 6

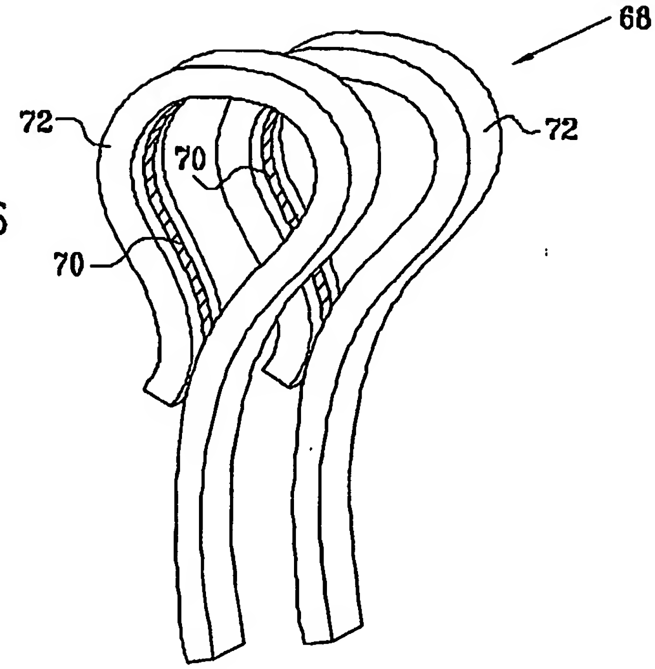


FIG. 7

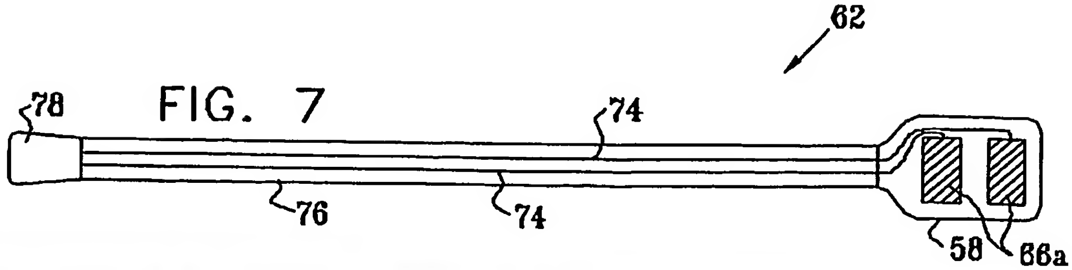


FIG. 8

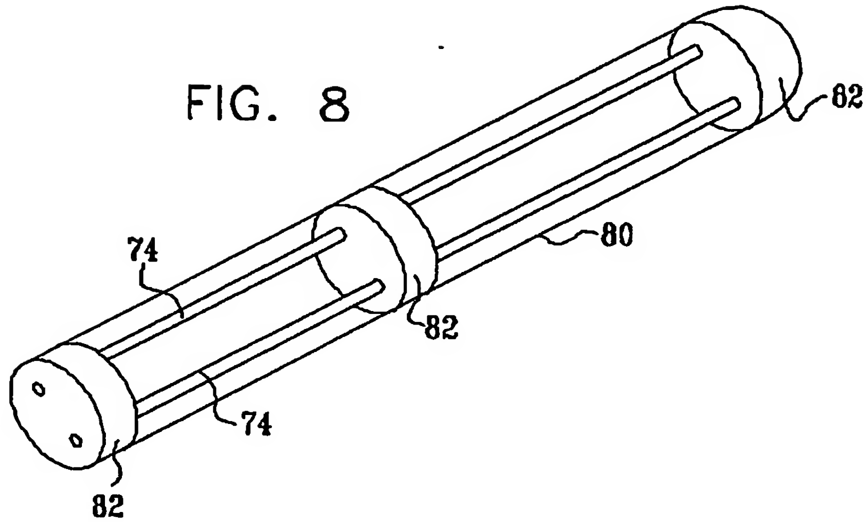


FIG. 9A

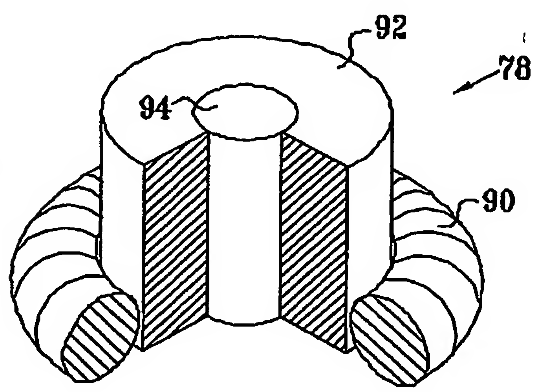


FIG. 9B

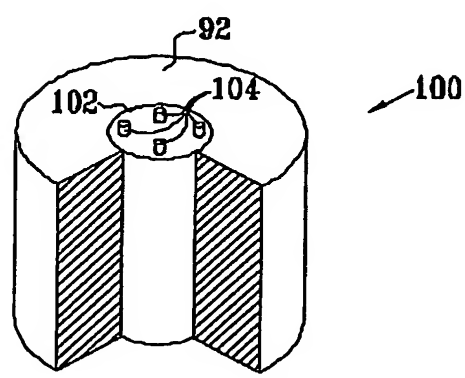


FIG. 10

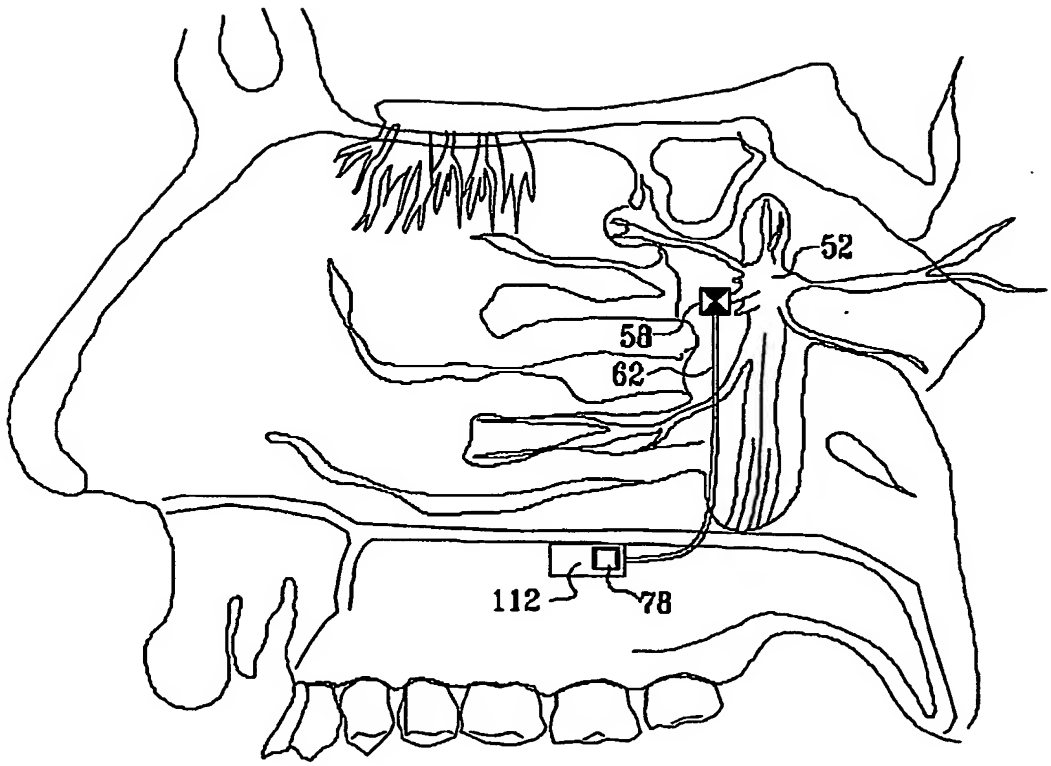


FIG. 11